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[54] Name of the invention: A composite drug used to treat viral myocarditis

[57] Abstract

This invention involves a composite drug used to treat viral myocarditis. This composite drug contains a certain amount of total alkaloids of Snphora angustifolia (Kuh-seng) and astragalus leaf saponins. In line with different drug applications and channels, different auxiliary additive substances can be used to prepare for a variety of dosage forms.

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1. A composite drug used to treat viral myocarditis. It is characterized in that its efficacious contents are the total alkaloids of Snphora angustifolia (Kuh-seng) and astragalus leaf saponins. The ratio between the total alkaloids of Snphora angustifolia (Kuh-seng) and regular astragalus leaf saponins is 1: 1 – 1: 5 or 1: 1 – 5: 1.
2. According to the composite drug described in Claim 1, it is characterized in that the total alkaloids of Snphora angustifolia (Kuh-seng) contains quinolizidine type alkaloids.
3. According to the composite drug described in Claim 2, it is characterized in that quinolizidine type alkaloids contain matrine.
4. According to the composite drug described in Claim 1, it is characterized in that astragalus leaf saponins contains contents of triterpenoid saponin.
5. According to the composite drug described in Claim 4, it is characterized in that triterpenoid saponin contains astragaloside IV.
6. According to the composite drug described in Claims 1, 2, 3, 4 and 5, it is characterized in that the optimum chosen ratio between total alkaloids of Snphora angustifolia (Kuh-seng) and astragalus leaf saponins is 1: 1.
7. According to the composite drug described in Claim 1, it is characterized in that this drug can be prepared in a variety of dosage forms, including tablets, capsules, guttage pills, liquoers, slow release pills, and injection agent.

Technical field

This invention involves a composite drug used to treat viral myocarditis. The efficacious contents of this drug are the total alkaloids of Snphora angustifolia extracted from Snphora angustifolia and other medical herbal plants, and astragalus leaf saponins extracted from astraglus.

Technical background

Viral myocarditis is a disease caused by virus and characterized by symptoms of myocarditis. The number of such cases has been on the rise in recent years, especially among young adults. This disease has become a common medical problem, which has posed a serious threat to humans, especially young adults.

At present, the major clinical treatment method for viral myocarditis in China and other countries is the utilization of common anti-virus drugs, immunocuppressants, interferons, and nutrient agents for cardiac muscle cells. But the curative effect is far from ideal.

Traditional Chinese Medicine has made a great difference in treating viral myocarditis. In China in recent years, the clinical application of Traditional Chinese Medicine has cured a far greater number of viral myocarditis patients than the aforesaid methods of Western Medicine. The majority of current treatment methods of Traditional Chinese Medicine, however, are prescribed soup medicines concocted by doctors themselves, such as pulse activating decoction, five ginseng soup, astragalus root heart comforting oral solution, heart muscle drink, etc. In Traditional Chinese Medicine, there is a dearth of advanced dosage forms that are convenient for administration.

The content of this invention

The purpose of this invention is to provide a composite drug used to treat vial myocarditis.

Based on the research into the efficacious components and pharmaceutical functionalities, this invention reconstitutes the total alkaloids of Snphora angustifolia extracted from Snphora angustifolia and other herbal plants, with astragalus leaf saponins extracted from astraglus. The inventors have found that the composite drug thus prepared exhibits an outstanding efficacy to treat viral myocarditis, thus accomplishing this invention.

The composite drug described in this invention contains the total alkaloids of Snphora angustifolia extracted from Snphora angustifolia and other medical herbal plants, and astragalus leaf saponins extracted from astraglus. Among those medical herbal components, the total alkaloids of Snphora angustifolia contain matrine, oxymatrine, sophocarpine, sophoridine and other alkaloid type substances similar to quinolizidine; astragalus leaf saponins contains astragaloside IV, acetylastragaloside I, isoastragaloside I, astramembrannine II and other substances similar to triterpenoid saponin.

In the composite drug of this invention, the ratio between the total alkaloids of Snphora angustifolia and astragalus leaf saponins is 1:1 – 1:5 or 1:1 – 5:1, with the optimum chosen ratio of 1:1.

In the composite drug described of this invention, the total alkaloids can be extracted from Snphora angustifolia or other medical herbal planted by means of regular alkaloids extraction and purification method through acid water or ethyl alcohol solvents. Astragalus leaf saponins can be extracted from astragalus by means of regular extraction and purification method of leaf saponins through ethyl alcohol – macroporous resin or n-butyl alcohol. For more detailed information about extraction and purification techniques, please refer to "Handbook on Extraction and Purification Methods for Chemical Components of Traditional Chinese Medicine" (Compiled by Yang Yun, Published by Traditional Chinese Medicine Publishing House, the First Edition, 1998)

The composite drug of this invention can be administered by means of regular clinical methods, such as oral administration, injection administration, skin administration and sticky plaster administration.

For the composite drug of this invention, all acceptable chemical additives can be added, including bulking agents, humectant agents, bond agents, disintegrating agents, surface active agents, thinner agents, lubricant agents.

In the composite drug of this invention, the main ratio between the total alkaloids of Snphora angustifolia and astragalus leaf saponins is 1:1 – 1:5 or 1 – 5:1. In line with different drug administration methods and channels, different auxiliary agents can be added to prepare for different dosage forms. For examples, a certain amount of hyprolose can be thrown in to prepare for tablets, a certain amount of Aerosil can be thrown in to prepare for capsules, a certain amount of tween 80 and injection water can be added to prepare for injection agent, etc. All regular pharmaceutical techniques can be used to prepare the composite drug of this invention for all kinds of chemical dosage forms, including regular dosage forms and slow release dosage forms, such as tablets, capsules, pills, oral solutions, dripping pills, slow release micro pills, injection agents, transdermal absorbing corks, suppositories, etc.

In the composite drug of this invention, the regular drug efficacy test and toxin test are adopted. The test results are described as follows:

The anti-virus test I outside the human body
Note: For the test method, please refer to "Test Methods for Modern Pharcology" (The second volume, P1427, Compiled by Zhang Juntian, Published by the Joint Publishing House of Beijing Medical University and China Xiehe Medical University, 1998 Edition)

Dilute BS1465 Wish cells into 2×10^5 / ml cell suspension solution, place the solution into the 96-hole Sunub, with 0.1 ml for each hole, and incubate the solution in 5%CO_2 at 37℃ for 24 hours, and then divide it into different groups:

Normal comparison group: add no drugs or virus. Viral comparison group: use 0.1 ml CVB_3 viral solution (100TCID50) infected cells, add no composite drug of this invention.

Drug administered group: add viral solution with the same titer into the incubated cells, let them absorb each at 37 ℃ for 2 hours, then throw in nutrient solution of the composite drug of this invention with different concentrations.

Let the three groups continue to hatch for 72 hours. When the viral comparison group shows pathological changes of +++ to ++++, measure the cell surviving volume by means of a neutral red dye.

The result: The two dosage groups of the composite drug of this invention exhibit an obvious role of anti-coxsackie B_3 virus. See Table 1 for details.

Table 1 Anti-Virus Test Outside Human Body

Groups	Cell surviving volume X ± SD (n=6)
Normal comparison group	0.52 ± 0.03
Virus comparison group	0.14 ± 0.02
High drug dosage administered group (200) μg / ml	0.47 ± 0.04**
Low drug dosage administered group (100) μg / ml	0.46 ± 0.02**

Note: Drug administered group vs virus group: **$P < 0.01$

The anti-virus test II inside the animal body

Note: For the test method, please refer to "Test Methods for Modern Pharcology" (The second volume, P1427, Compiled by Zhang Juntian, Published by the Joint Publishing House of Beijing Medical University and China Xiehe Medical University, 1998 Edition)

Take 70 BABL / C small rats and randomly put them into 4 groups:

Normal comparison group: 10 small rats. Do not administer to them the composite drug of this invention, nor inoculate them with virus, just give each of them an equal amount of distilled water.

Virus comparison group: 20 small rats. Inoculate each of them inside the belly with 0.5 ml CVB3 viral solution ($1000TCID_{50}$).

Drug administered group:

High drug dosage: 20 small rats. Inoculate each of them with virus by means of the aforesaid method, administer to them the composite drug of this invention in the amount of 300mg / kg.d by means of intragastric administration every day, for 10 days on a row.

Low drug dosage: 20 small rats. Inoculate each of them with virus by means of the aforesaid method, and administer to them the composite drug of this invention for an amount of 200mg / kg.d

Observe and record the conditions of the drug administered (feeding) group, including the animals' spirit, appetite, fur color, activities as well as possible death.

The result: The two dosage groups of the composite drug of this invention can obviously lower viral myocarditis rate and death rate caused by coxsackie B_3 virus. See Table 2 for details.

Table 2 The anti-virus test II inside the animal body

Group	Number of animal	Disease rate (# of cases)	Death rate (# of cases)
Normal comparison group	10	0 (0)	0 (0)
Virus comparison group	20	90% (18)	50% (10)
High drug dosage group	20	40% (8) **	10% (2) **
Low drug dosage group	20	45% (9) **	15% (3) *

Note: Drug administered group vs virus group: *P < 0.05, ** P < 0.01

The anti-virus test III for the composite drug of this invention

Note: For test methods, please refer to "The Technical Requirements for New Drugs of Traditional Chinese Medicine" (P22, Promulgated by the State Drug Administration, 2000)

Take 140 Kunming Species small rats, half male and half female, randomly put them into 7 groups. Administer to them the composite drug of this invention orally and by injection in the belly. Observe them for 7 days, record toxic reactions, body weight changes and possible deaths. Measure 50% death causing dosage (LD_{50}) of small rats by means of Bliss method. The result shows 9320mg / kg for oral administration, 261mg / kg for belly injection. This result shows a low toxicity of the drug.

Specific embodiment method

Next we will make further description of this invention according to the specific embodiment example, but we shall not place any restraint.

Embodiment Example 1

Select the composite drug of this invention and additive agents in the following amount:

Total alkaloids of Snphora angustifolia	100 g
Sstragalus leaf saponins	100g
Hyprolose	130g
Aerosil	30g
Pregelatinized starch	20g
Magnesium stearate	an appropriate amount
Prepare for	1000 granules

Mix evenly the above composite drug of this invention and additives, use 10% pregelatinized starch slurry as a bond agent, make tablets by wet method, dry them, throw in an appropriate amount of magnesium stearate, mix the compound, press them into tablets.

Embodiment Example 2

Select the composite drug of this invention and additive agents in the following amount:

Total alkaloids of Snphora angustifolia	160 g
Sstragalus leaf saponins	40g
Hyprolose	60g
Aerosil	30g
Ethanol	an appropriate amount
Magnesium stearate	an appropriate amount
Prepare for	1000 granules

Mix evenly the above composite drug of this invention with hyprolose and Aerosil , use an appropriate amount of 70% ethanol as an humectant agent, make tablets by wet method, filter tablets through 40-hole sieve, dry them, throw in an appropriate amount of magnesium stearate, mix the compound, place them into capsules.

Embodiment Example 3

Select the composite drug of this invention and the additive agents in the following amount:

Total alkaloids of Snphora angustifolia	50 g
Sstragalus leaf saponins	150g
Methocel E_{50}	100g
Methocel K4m	60g
Milk sugar	20g
Hyprolose	30g
PVP K30	an appropriate amount
Aerosil	30g
Magnesium stearate	an appropriate amount
Prepare for	1000 granules

Mix evenly the above composite drug of this invention with methocel, milk sugar and hyprolose, use an appropriate amount of 10% PVP ethanol solution as an bond agent, make tablets by wet method, dry them, throw in an appropriate amount of magnesium stearate, mix the compound, press the compound into slow release pills.

Embodiment Example 4

Select the composite drug of this invention and additive agents in the following amount:

Total alkaloids of Snphora angustifolia	167 g
Astragalus leaf saponins	33g
Polyethylene glycol 6000	350g
Stearic acid	5%
Prepare for	1000 granules

Grind the total alkaloids of Snphora angustifolia and astragalus leaf saponins into fine granules (sift them through 100-hole sieve). Mix the drug granules evenly with Polyethylene glycol 6000 and Stearic acid, stir the compound as it is being heated (90 – 100°C). When the compound is completely dissolved, maintain the drug liquid at 80 – 85°C and quickly drop it at a controlled rate into the condensate of methylsilicone oil so that the drug liquid can be condensed into pills.

Embodiment Example 5

Select the composite drug of this invention and additive agents in the following amount:

Total alkaloids of Snphora angustifolia	1.7 g
Astragalus leaf saponins	8.3g
Cane sugar	200g
Preservative	An appropriate amount
Distilled water	An appropriate amount
Prepare for	1000 ml

Take an appropriate amount of distilled water, add in the total alkaloids of Snphora angustifolia and astragalus leaf saponins, stir the compound as it is heated to let the compound dissolve. Filter the compound drug solution. Place cane sugar and preservative into distilled water as it is heated to let them dissolve, pour the above drug solution slowly into the distilled water while stirring it. Throw in the full amount of distilled water, mix evenly, store the liquid compound in a cooler, filter it, seal it in a container and sterilize it, thus obtaining the oral solution.

Embodiment Example 6

Select the composite drug of this invention and additive agents in the following amount:

Total alkaloids of Snphora angustifolia	5 g
Astragalus leaf saponins	5 g
Tween 80	An appropriate amount
Injection water	An appropriate amount
Prepare for	1000 ml

Take an appropriate amount of injection water, add in the total alkaloids of Snphora angustifolia and astragalus leaf saponins, heat the compound and stir it so that it will dissolve completely. Throw in 4% tween 80, stir thoroughly, filter the compound, add in hydrochloric acid to adjust pH value to 6.8. Throw in the full amount of injection water. Ultrafiltrate the solution by hollow cored fibre, then fine filter the solution, and sterilize it to obtain the injection agent.

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权利要求书 1 页 说明书 7 页

[54] 发明名称 一种治疗病毒性心肌炎的药物组合物

[57] 摘要

本发明涉及一种治疗病毒性心肌炎的药物组合物，该药物组合物含有一定比例苦参总生物碱和黄芪总皂苷，根据不同的给药途径，配有不同的辅料制成不同的剂型。

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一种治疗病毒性心肌炎的药物组合物

技术领域

本发明涉及一种治疗病毒性心肌炎的药物组合物，该药物组合物的有效组分为从苦参或其它植物药中提取的苦参总生物碱和从黄芪中提取的黄芪总皂苷。

背景技术

病毒性心肌炎是一种由病毒感染所致的以心肌炎症病变为主的疾病。近十多年来发病率上升很快，尤其是青壮年患者迅速增加，已成为严重危害人类，尤其是中青年健康的新的常见病。

目前，国外及国内西医临床治疗病毒性心肌炎的主要方法是使用普通抗病毒药、免疫抑制剂、干扰素及心肌细胞营养剂等，但疗效并不理想。

中药在治疗病毒性心肌炎中显示了很大的优势。近年来国内临床用中医药治疗该病的治愈率远远高于上述西药疗法。但目前绝大部分为医生自拟的处方汤药，如生脉饮，五参汤，芪冬颐心口服液，心肌饮等，缺乏剂型先进、服用方便的中药制剂。

发明内容

本发明的目的就是提供一种治疗病毒性心肌炎的药物组合物。

本发明在有效成分和药理作用研究的基础上，将从苦参或其它植物药中提取的苦参总生物碱与从黄芪中提取的黄芪总皂苷配伍，发现该组合物具有优良的抗病毒性心肌炎功效，从而完成了本发明。

本发明的药物组合物包含从苦参或其它植物药中提取的苦参总生物碱和从黄芪中提取的黄芪总皂苷。其中，苦参总生物碱包含苦参碱(matrine)、氧化苦参碱(oxymatrine)、槐果碱(sophocarpine)、槐定碱(sophoridine)等喹啉里西啶(quinolizidine)类生物碱成分，黄芪总皂苷包含黄芪甲苷(astragaloside IV)、乙酰黄芪苷 I (acetylastragaloside I)、异黄芪苷 I (isoastragaloside I)、黄芪皂苷乙(astramembrannin II)等三萜皂苷类成分。

在本发明的药物组合物中，苦参总生物碱与黄芪总皂苷的比例为 1:1～1:5

1. 一种治疗病毒性心肌炎的药物组合物，其特征在于它包含的有效组分为苦参总生物碱和黄芪总皂苷，苦参总生物碱与黄芪总皂苷的比例为 1：1～1：5 或 1：1～5：1。

2. 根据权利要求 1 所述的药物组合物，其特征在于其苦参总生物碱包含喹啉里西啶（quinolizidine）类生物碱。

3. 根据权利要求 2 所述的药物组合物，其特征在于其喹啉里西啶类生物碱包含苦参碱（matrine）。

4. 根据权利要求 1 所述的药物组合物，其特征在于其黄芪总皂苷包含三萜皂苷类成分。

5. 根据权利要求 4 所述的药物组合物，其特征在于其三萜皂苷包含黄芪甲苷（astragaloside IV）。

6. 根据权利要求 1，2，3，4，5 所述的药物组合物，其特征在于其苦参总生物碱与黄芪总皂苷的优选比例为 1：1。

7. 根据权利要求 1 所述的药物组合物，其特征在于可制成的剂型包括：片剂，胶囊剂，滴丸剂，溶液剂，缓控释剂及注射剂。

或 1:1～5:1，优选比例为 1:1。

在本发明的药物组合物中，苦参总生物碱可采用酸水或醇溶剂等常规的生物碱提取纯化方法从苦参或其它植物药中提取得到；黄芪总皂苷可采用醇—大孔树脂或正丁醇等常规的皂苷提取纯化方法从黄芪中提取得到。详细提取纯化工艺可参考《中药化学成分提取分离手册》（杨云主编，中国中医药出版社，1998 年第一版）。

本发明的药物组合物可通过临床上常用的各种给药途径给药，如口服给药，注射给药，皮肤给药和粘膜给药。

本发明的药物组合物可选用药学上可接受的各种附加剂，包括填充剂，湿润剂，粘合剂，崩解剂，表面活性剂，稀释剂，润滑剂等。

本发明的药物组合物以苦参总生物碱与黄芪总皂苷之比为 1:1~1:5 或 1~5:1 为主，再根据不同的给药途径配有不同的辅剂制成不同的剂型，例如：加入一定量羟丙纤维素等制成片剂；加入一定量微粉硅胶等制成胶囊剂；制成针剂采用加适量吐温 80，再加注射用水，等等。采用本领域常规制剂技术即可把本发明药物组合物制成药学上的各种制剂，包括普通制剂和缓（控）释制剂，如片剂、胶囊、颗粒剂、口服液、滴丸、缓释微丸、注射剂、透皮吸收剂、栓剂等。

本发明配制的药物组合物采用常规的药效及毒性试验经试验结果如下：

本发明药物组合物的体外抗病毒试验 I

注：试验方法参考《现代药理实验方法》（下册，P1427，张均田主编，北京医科大学中国协和医科大学联合出版社，1998 年版）

将人羊膜细胞株稀释成 2×10^5 个/ml 的细胞悬液，加至 96 孔培养板中，每孔 0.1 ml，37℃，5%CO_2 中培养 24h 后分组：

正常对照组：不加任何药物及病毒。病毒对照组：用 0.1 ml 的 CVB_3 病毒液（100TCID50）感染细胞，不加本发明药物组合物。

给 药 组：在经过培育的细胞中加入相同滴度的病毒液，37℃吸附 2h 分别加含不同浓度本发明药物组合物的培养液。

三组继续孵育 72h，待病毒对照组病变达+++至++++时，用中性红染料法测细胞存活量。

结果：本发明药物组合物两个剂量组均有显著的抗柯萨奇B_3病毒的作用，见表1。

表1 体外抗病毒试验结果

组 别	细胞存活量 X±SD（n=6）
正常对照组	0.52±0.03
病毒对照组	0.14±0.02
给药高剂量组（200μg/ml）	0.47±0.04**
给药低剂量组（100μg/ml）	0.46±0.02**

注：给药组与病毒组比较：**P<0.01。

本发明药物组合物的体内抗病毒试验II

注：试验方法参考《现代药理实验方法》（下册，P1467，张均田主编，北京医科大学中国协和医科大学联合出版社，1998年版）。

取BABL/C小鼠70只，随机分成4组：

正常对照组：10只，不给本发明药物组合物，也不接种病毒，只给等量蒸馏水。

病毒对照组：20只，每只腹腔接种0.5ml CVB_3病毒液（$1000TCID_{50}$）。

给 药 组：高剂量：20只，同上法接种CVB_3病毒液，同日按300mg/kg·d灌胃给予本发明药物组合物，连续10天。

低剂量：20只，同上法接种病毒液及给予本发明药物组合物，剂量为200mg/kg·d。

观察记录给药（饲养）期间动物的精神状态、饮食、毛色、活动及死亡等情况。

结果：本发明药物组合物两个剂量组均能显著降低由柯萨奇B_3病毒引起的病毒性心肌炎小鼠的发病率和死亡率，见表2。

表 2 体内抗病毒试验结果

组别	动物数（只）	发病率（例数）	死亡率（例数）
正常对照组	10	0（0）	0（0）
病毒对照组	20	90%（18）	50%（10）
给药高剂量组	20	40%（8）**	10%（2）**
给药低剂量组	20	45%（9）**	15%（3）*

注： 给药组与病毒组比较：* P<0.05, ** P<0.01

本发明药物组合物的毒性试验 III

注：试验方法参考《中药新药研究的技术要求》（P22，国家药品监督管理局颁布，2000 年）

取昆明种小鼠 140 只，雌雄各半，随机分成 7 组，分别口服和腹腔注射本发明药物组合物，连续观察 7 天，记录动物毒性反应、体重变化及死亡情况，用 Bliss 法计算小鼠的半数致死量（LD_{50}），结果为口服 9320mg/kg，腹腔注射 261mg/kg，说明毒性极低。

具体实施方式

下面结合具体实施例对本发明作进一步阐述，但不对其有任何限制。

实施例 1

选用下列用量的药物组合物与附加剂：

苦参总生物碱	100 g
黄芪总皂苷	100 g
羟丙纤维素	130 g
微粉硅胶	30 g
预胶化淀粉	20 g
硬脂酸镁	适量
制成	1000 粒

将上述药物组合物与附加剂混合均匀，用 10%预胶化淀粉浆作为粘合剂，湿法制粒，烘干，加入适量硬脂酸镁混合，压制成片剂。

实施例 2

选用下列用量的药物组合物与附加剂：

苦参总生物碱	160 g
黄芪总皂苷	40 g
羟丙纤维素	60 g
微粉硅胶	30 g
乙醇	适量
硬脂酸镁	适量
制成	1000 粒

将上述药物组合物与羟丙纤维素及微粉硅胶混合，用适量 70%乙醇做湿润剂，湿法制粒，过 40 目筛制成颗粒，烘干，加入硬脂酸镁，混合，装入硬胶囊。

实施例 3

选用下列用量的药物组合物与附加剂：

苦参总生物碱	50 g
黄芪总皂苷	150 g
羟丙甲纤维素（Methocel E_{50}）	100 g
羟丙甲纤维素（Methocel K_{4m}）	60 g
乳糖	20 g
羟丙纤维素	30 g
聚乙烯吡咯烷酮（PVP K30）	适量
硬脂酸镁	适量
制成	1000 片

将上述药物组合物与羟丙甲纤维素、乳糖及羟丙纤维素混合均匀，加入 10% PVP 乙醇溶液作粘合剂，湿法制粒，烘干，加硬脂酸镁，混匀，压制得缓释片。

实施例 4

选用下列用量的药物组合物与附加剂：

苦参总生物碱	167 g
黄芪总皂苷	33 g
聚乙二醇 6000	350 g
硬脂酸	5%
制成	1000 粒

将苦参总生物碱和黄芪总皂苷研细(100 目筛)，与聚乙二醇 6000 和硬脂酸混匀，边搅拌边加热（90～100℃），待全部熔化后，料液在 80～85℃保温条件下控速滴入甲基硅油冷凝液中，冷凝成丸。

实施例 5

选用下列用量的药物组合物与附加剂：

苦参总生物碱	1.7 g
黄芪总皂苷	8.3 g
蔗糖	200 g
防腐剂	适量
蒸馏水	适量
制成	1000 ml

取蒸馏水适量，加入苦参总生物碱和黄芪总皂苷，边加热边搅拌使溶解，过滤。另将蔗糖和防腐剂用蒸馏水加热溶解，在搅拌下缓缓加入上述溶液中，加蒸馏水至全量，混匀，冷藏，过滤，灌封，灭菌，得口服液。

实施例 6

选用下列用量的药物组合物与附加剂：

苦参总生物碱	5 g
黄芪总皂苷	5 g
吐温 80	适量
注射用水	适量
制成	1000 ml

取适量注射用水，加入苦参总生物碱和黄芪总皂苷，加热，搅拌使充分溶解，加入 4%吐温 80，充分搅匀，过滤，加盐酸调 pH 至 6.8，加注射用水至足量，中空纤维超滤，精滤，灌封，灭菌，得注射液。